

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Sun, LuZhe eRA COMMONS USER NAME (credential, e.g.,

agency login): SUNL01

POSITION TITLE: Professor, Dielmann Endowed Chair in Oncology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Shanghai Fisheries College, PRC	B.S.	01/82	Fishery Science
Rutgers University	M.S.	06/85	Physiology
Rutgers University	Ph.D.	01/90	Physiology
Baylor College of Medicine	Post-doc	02/90-03/92	Mol. Cancer Biology

A. Personal Statement

I have a long-standing commitment to cancer research and to the training of young investigators. Two Xiangya Medical students have completed their two-year research program in my lab. One Xiangya Medical student is currently conducting his research in my lab. I served for six years as the inaugural Leader of Cell and Molecular Biology Track of our graduate school's Integrated Multidisciplinary Graduate Program in charge of the organization and operation of the track. I have trained one MS student, eight Ph.D. students, including two currently in my lab, mentored seventeen postdoctoral fellows, and served as Honor Thesis Advisor for three undergraduate students. My trainees obtained various awards including a predoctoral training grant from DOD, and published multiple manuscripts in peer-reviewed journals, and got prestigious placements in academia or biotech companies. I have served as the mentor for several basic and physician scientists, who have successfully obtained grants including a K08 Award from NCI and Voelcker Young Investigator Awards on Translational Science from Voelcker Foundation. In addition, I am currently serving as the director for a NIH/NCI T32 training grant for our Cancer Biology Training Program. My approaches in training students and young scientists are (1) to encourage independent thinking and collaboration, (2) to provide opportunities for intellectual and technical growth, (3) to foster personal strengths, and (4) to make myself available for research meetings and consultations. The opportunity of being able to interact with trainees to make scientific discovery is truly the most rewarding experience I derive from my profession. My research is focused on molecular mechanisms of tumorigenesis and metastasis, and novel experimental therapeutics in various models of breast, prostate, and liver cancers for the past twenty-five years. The effect of aging and xenoestrogen on mammary stem cell function and tumorigenesis is a new research direction. My research has been continuously funded, since my First Award as a Research Assistant Professor, by R01 and P01 grants from NIH, IDEA and Concept Awards from DOD Breast and Prostate Cancer Research Programs, InvestigatorInitiated Research Award from CPRIT, and grants from private foundations.

B. Positions and Honors**Positions and Employment**

4/92-9/92 Research Associate, Department of Biochemistry and Molecular Biology, Medical College of Ohio, Toledo, Ohio.

9/92-3/95	Research Assistant Professor, Department of Biochemistry and Molecular Biology, Medical College of Ohio, Toledo, Ohio.
4/95-6/99	Assistant Professor, Department of Pharmacology, College of Medicine, University of Kentucky, Lexington, KY.
7/99	Associate Professor with tenure, Department of Pharmacology, College of Medicine, University of Kentucky, Lexington, KY.
8/99-8/01	Associate Professor with tenure, Department of Surgery, University of Texas Health Science Center, San Antonio, TX.
9/01-8/04	Associate Professor with tenure, Department of Cellular & Structural Biology, University of Texas Health Science Center, San Antonio, TX.
9/04-present	Professor with tenure, Department of Cellular & Structural Biology, University of Texas Health Science Center, San Antonio, TX.
9/09-present	Dielmann Endowed Chair in Oncology, Associate Director for Basic Research at Cancer Therapy and Research Center, Univ. of TX Health Science Ctr., San Antonio, TX.

Honors and Other Professional Activities

1987-1988	Charles & Johanna Busch Predoctoral Fellowship at Rutgers University
1988-1989	Anne B. and H. Leathem Scholarship at Rutgers University
1994-1999	R29 First Award, National Cancer Institute, NIH
1994-present	Member, American Association for Cancer Research
1995-present	Member, American Society for Biochemistry and Molecular Biology
1999-2017	Reviewer (ad hoc) for the US Dept. of Defense Breast Cancer Research Program
2001-2016	Reviewer (ad hoc) for the US Dept. of Defense Prostate Cancer Research Program
2003, 2016	Reviewer for NIH/NCI Subcommittee I-Career Development study section (3 meetings)
2003-2008	Charter member in NIH/NCI Cancer Biomarker Study Section
2005	Reviewer for NIH/NCI Oncology Fellowship and AREA Study Section (2 meetings)
2006	Reviewer for NIH/NCI Drug Discovery and Molecular Pharmacology Study Section
2007	Reviewer for NIH/NCI PO1 cluster review in Cellular & Tissue Biology SEP
2008-2009	Reviewer for NIH/NCI Tumor Progression and Metastasis Study Section
2010-2017	Reviewer for NIH/NCI Basic Mechanisms of Cancer Therapeutics Study Section (5 meetings)
2011-2014	Charter member in NIH/NCI Tumor Progression and Metastasis Study Section
2015	Reviewer for NIH/NCI Cancer Molecular Pathology Study Section (1 meeting)
2015-present	Investigator of Clayton Foundation for Research
2015-present	AAAS Fellow, elected by the Council of American Association for the Advancement of Science

C. Contribution to Science

1. Discovery of the tumor suppressor function of TGF β receptors. Transforming growth factor-beta (TGF β) was initially discovered as a growth factor with transforming activity in mid 1980's, but was later found to inhibit proliferation of various types of cells by blocking cell cycle progression suggesting its pathway may have tumor suppressive function. When I was a junior faculty member working with Dr. Michael Brattain in Medical College of Ohio, our laboratory was among the first to show the tumor suppressive function of TGF β type II receptor (*TGFBR2*) in human breast and colon cancer cells. Dr. Brattain's PhD student, J. Wang, working with me identified a group of human colon cancer cell lines that did not express *TGFBR2* mRNA. These cell lines were then recognized by Dr. Sanford Markowitz in Case Western Reserve University to be derived from hereditary nonpolyposis colorectal cancer patients with DNA mismatch repair deficiency and high microsatellite instability. This led to the discovery of *TGFBR2* being a bona fide tumor suppressor in collaboration with Dr. Vogelstein's lab. My own laboratory also demonstrated the tumor suppressive function of the type III receptor/betaglycan of TGF β (*TGFBR3*) subsequently.
 - a. **Sun, L-Z.,** G. Wu, J.K.V. Willson, E. Zborowska, J. Yang, I. Rajakarunanayake, J. Wang, L.E. Gentry, X.-F. Wang, and M.G. Brattain. Expression of transforming growth factor β type II receptor leads to reduced malignancy in human breast cancer MCF-7 cells. *J. Biol. Chem.* 269:26449-26455, 1994.
<http://www.ncbi.nlm.nih.gov/pubmed/7929366>

- b. Markowitz, S., J. Wang, L. Myeroff, R. Parsons, **L-Z. Sun**, J. Lutterbaugh, R.S. Fan, E. Zborowska, K.W. Kinzler, B. Vogelstein, M. Brattain, and J.K.V. Wilson. Inactivation of Type II TGF β Receptor in Colon Cancer Cells with Microsatellite Instability. *Science* 268: 1336-1338, 1995.
<http://www.ncbi.nlm.nih.gov/pubmed/7761852>
 - c. Wang*, J., **L-Z. Sun***, L. Myeroff, X.-F. Wang, L.E. Gentry, J. Yang, J. Liang. E. Zborowska, S. Markowitz, J.K.V. Willson, and M.G. Brattain. Demonstration that mutation of the type II TGF β receptor inactivates its tumor suppressor activity in RER positive colon carcinoma cells. *J. Biol. Chem.*, 270: 22044-22049, 1995. <http://www.ncbi.nlm.nih.gov/pubmed/7665626>.
 - d. **Sun, L-Z.** and C. Chen. Expression of transforming growth factor β type III receptor suppresses tumorigenicity of human breast cancer MDA-MB-231 cells. *J. Biol. Chem.* 272:25367-25372, 1997.
<http://www.ncbi.nlm.nih.gov/pubmed/9312157>
2. Demonstration of the paradoxical role of TGF β in the regulation of tumor progression. My early research as an independent investigator was focused on elucidation of autocrine and paracrine roles of TGF β signaling pathway in driving tumor progression. My lab was the first to report the suppression of human telomerase reverse transcriptase transcription by autocrine TGF β as a novel mechanism of its tumorsuppressive function in human cancer cells. Subsequently, we found that abrogation of TGF β signaling as an autocrine factor in cancer cells and as a paracrine factor in cancer stromal cells blocked tumor progression demonstrating a tumor-promoting role of TGF β signaling.
- a. Chen, C., X. Wang, and **L-Z. Sun**. Expression of transforming growth factor beta (TGF β) type III receptor restores autocrine TGFbeta1 activity in human breast cancer MCF-7 Cells. *J. Biol. Chem.* 272:12862-12867, 1997. <http://www.ncbi.nlm.nih.gov/pubmed/9139748>
 - b. Yang, H., S. Kyo, M. Takatura, and **L-Z. Sun**. Autocrine transforming growth factor β suppresses telomerase activity and transcription of human telomerase reverse transcriptase in human cancer cells. *Cell Growth & Differentiation*. 12:119-127, 2001. <http://www.ncbi.nlm.nih.gov/pubmed/11243466>
 - c. Lei, X., A. Bandyopadhyay, T. Le, and **L-Z. Sun**. Autocrine TGF β activity supports growth and survival of human breast cancer MDA-MB-231 cells. *Oncogene* 21:7514-7523, 2002.
<http://www.ncbi.nlm.nih.gov/pubmed/12386814>
 - d. Verona, Erik V., Abdel Elkahoun, Junhua Yang, Abhik Bandyopadhyay, I-Tien Yeh, and **L-Z. Sun**. Transforming growth factor- β Signaling in prostate stromal cells supports prostate carcinoma growth by upregulating stromal genes related to tissue remodeling. *Cancer Res.* 67:5737-5746, 2007.
<http://www.ncbi.nlm.nih.gov/pubmed/17575140>
3. Development of TGF β inhibitors as novel anti-TGF- β therapeutics. As TGF β signaling was found to drive late-stage tumor progression, particularly metastasis, several pharmaceutical companies started to search for and publish small molecule TGF β receptor kinase inhibitors in early 2000. My lab focused on utilizing and developing soluble TGF β receptors as pan TGF β traps/inhibitors. We were the first to use a soluble TGF β type III receptor/betaglycan and a small inhibitor of TGF β type I receptor kinase as therapeutic agents to inhibit tumor angiogenesis and metastasis in xenograft models of breast and prostate cancer. We also developed a novel soluble chimeric TGF β receptor, BGeRII, as a potent pan TGF β inhibitor with a US Patent. My lab was among the first to show that chemo-drugs such as doxorubicin can stimulate TGF β /Smad signaling and the combination of a TGF β inhibitor with doxorubicin was significantly more efficacious than either drug alone in attenuating breast tumor growth and metastasis.
- a. Bandyopadhyay, A., F. Lopez-Casillas, S.N. Malik, J.L. Montiel, V. Mendoza, J. Yang, and **L-Z. Sun**. Antitumor activity of a recombinant soluble betaglycan in human breast cancer xenograft. *Cancer Res.* 62:4690-4695, 2002. <http://www.ncbi.nlm.nih.gov/pubmed/12183427>
 - b. Bandyopadhyay, A., J.K. Agyin, L. Wang, Y. Tang, X. Lei, B.M. Story, J.E. Cornell, B.H. Pollock, G.R. Mundy, and **L-Z. Sun**. Inhibition of pulmonary and skeletal metastasis by a TGF β Type I receptor kinase inhibitor. *Cancer Res.* 66:6714-6721, 2006. <http://www.ncbi.nlm.nih.gov/pubmed/16818646>
 - c. **L-Z. Sun** and A.P. Hinck. Antagonizing TGF-beta activity with various ectodomains of TGF-beta receptors used in combination or as fusion proteins. US Patent No. 7,795,389 (Serial No: 11/238,172), Sept. 14, 2010.

- d. Bandyopadhyay, Abhik, Long Wang, Joseph Aguin, Yuping Tang, Shu Lin, I-Tien Yeh, Keya De, and **L-Z. Sun**. Doxorubicin in combination with a small TGF β inhibitor: a potential novel therapy for metastatic breast cancer in mouse models. *PLoS ONE*, 5(4):e10365, 2010.
<http://www.ncbi.nlm.nih.gov/pubmed/20442777>
4. Development of a GFP-based assay for measuring DNA mismatch repair activity in live cells. Our discovery of the mutation of *TGFBR2* in DNA mismatch repair (MMR) deficient colon cancer cells coincided with the discovery and the use of the enhanced green fluorescent protein (EGFP) for biological research in mid 90's. At that time, MMR activity was mainly measured in cell nuclear extracts. There was no quick and efficient assay for measuring DNA MMR activity in live cells. My PhD student, Yong Zhu constructed an EGFP-based plasmid expression system for measuring MMR activity in live cells starting in mid 90's. After extensive testing and modifications, our system was published and provided to investigators from over fifty institutions worldwide for DNA MMR research.
 - a. Lei, X., Y. Zhu, A. Tomkinson, and **L-Z. Sun**. Measurement of DNA mismatch repair activity in live cells. *Nucleic Acids Res.* 32 (12): e100, 2004. <http://www.ncbi.nlm.nih.gov/pubmed/15249596>
 - b. Zhou, B., C. Huang, J. Yang, J. Lu, Q. Dong, and **L-Z. Sun**. Preparation of heteroduplex EGFP plasmid for in vivo mismatch repair activity assay. *Anal. Biochem.* 388:167-169, 2009.
<http://www.ncbi.nlm.nih.gov/pubmed/19248754>
5. Development of an *in vitro* assay for the identification and quantification of mammary stem and progenitor cells, and demonstration of early neoplastic lesion formation by mammary stem-like cells. My lab for the first time developed an *in vitro* sphere formation and differentiation (SFD) assay, which can be used as a reliable alternative to the *in vivo* repopulation assay for the qualification and quantification of mammary stem and progenitor cells. Using our novel SFD assay, we were the first to characterize mammary stem/progenitor cells in common marmosets and to show that aging-associated or xenoestrogen bisphenol A-induced mammary neoplasia was mediated by stem-like cells in mice.
 - a. Dong, Q., D. Wang, A. Bandyopadhyay, H. Gao, K. Moncada, K. Hildreth, V.I. Rebel, C.A. Walter, C. Huang, **L-Z. Sun**. Mammospheres from murine mammary stem cell-enriched basal cells: clonal characteristics and repopulating potential. *Stem Cell Research*, 10:396-404, 2013.
<http://www.ncbi.nlm.nih.gov/pubmed/23466563>
 - b. Wang, D., Hui Gao, Abhik Bandyopadhyay, Anqi Wu, I-Tien Yeh, Yidong Chen, Yi Zou Changjiang Huang, Christi A. Walter, Qiaoxiang Dong, **Lu-Zhe Sun**. Pubertal Bisphenol A Exposure Alters Murine Mammary Stem Cell (MaSC) Function Leading to Early Neoplasia in Regenerated Glands. *Cancer Prev Res.* 7(4): 445-455, 2014. <http://www.ncbi.nlm.nih.gov/pubmed/24520039>, featured in the cover of the issue: <http://cancerpreventionresearch.aacrjournals.org/content/7/4.cover-expansion>
 - c. Wu, A., Qiaoxiang Dong, Hui Gao, Yuanshuo Shi, Yuanhong Chen, Fuchuang Zhang, Abhik Bandyopadhyay, Danhan Wang, Karla M. Gorena, Changjiang Huang, Suzette Tardif, Peter W. Nathanielsz, and **Lu-Zhe Sun**. Characterization of mammary epithelial stem/progenitor cells and their changes with aging in common marmosets. *Sci. Rep.* 6:32190, 2016. doi: [10.1038/srep32190](https://doi.org/10.1038/srep32190)
 - d. Dong, Q., Hui Gao, Yuanshuo Shi, Fuchuang Zhang, Xiang Gu, Anqi Wu, Danhan Wang, Yuanhong Chen, Abhik Bandyopadhyay, I-Tien Yeh, Benjamin J. Daniel, Yidong Chen, Yi Zou, Vivienne L. Rebel, Christi A. Walter, Jianxin Lu, Changjiang Huang, **Lu-Zhe Sun**. Aging is associated with an expansion of CD49^{hi} mammary stem cells that show a decline in function and increased transformation potential. *Aging*, 2016. doi: [10.18632/aging.101082](https://doi.org/10.18632/aging.101082)

Complete List of Published Work:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1VkbqXW27j/bibliography/41562583/public/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

R01 ES022057

Sun (PI)

08/23/2012-4/30/2017

National Institute of Environmental Health Sciences

Effect of bisphenol A exposure on mammary stem cell function and transformation

The major goal of the project is to determine the effect of bisphenol A alone or in combination with irradiation or obesity on the function of murine and primate mammary stem/progenitor cells and on mammary tumorigenesis.
Role: PI

R01 CA172886-01A1 Sun & Hinck (Multi-PI) 07/01/2013-05/31/2017

National Cancer Institute

Inhibition of the tumor-promoting effects of TGF-beta in advanced prostate cancer

The major goals are to construct and produce protein-based anti-transforming Growth Factor β (TGF β) inhibitors and test their efficacy in blocking prostate cancer progression by stimulating host anti-tumor immunity.

Role: Contacting PI (starting Sept. 1, 2015)

P30 CA-54174 Thompson (PI) 09/01/14 – 08/31/19

National Cancer Institute

This is a Cancer Center Support Grant that provides infrastructure support to members of the cancer center for conducting their cancer-related research.

Role: Associate Director for Translational Research

R01 CA179120-01A1 Rao (PI) 02/2015 - 01/2020

National Cancer Institute

MicroRNAs: Safe and effective therapeutic adjuvants for treating drug resistant

The major goal is to test the hypothesis that miRNAs are effect therapeutic adjuvants to treat drug resistant triple negative breast cancers. Role: Co-Investigator

R01 CA192564-01A1 Sun (PI) 09/01/15 – 08/31/20

National Cancer Institute

Aging mammary stem cells and breast cancer prevention

The major goals are to investigate the potential utility of Rapamycin and other anti-inflammatory agents for the prevention of the transformation of murine and human mammary stem cells. Role: PI

R01 CA196214-01A1 Jiang and Sun (Multi-PI) 02/01/16 - 01/31/21

National Cancer Institute

Connexin hemichannels in suppression of breast cancer bone metastasis

The major goals are to determine the mechanisms of connexin 43 hemichannel-mediated inhibition of breast cancer-induced bone metastasis and the role of ATP receptors in mediating the crosstalk between osteocytes and breast cancer cells.

Role: Multi-PI

T32CA148724 -06 Sun (PI) 08/01/2016-07/31/2021

National Cancer Institute

Cancer Biology Training Program

The major goal of the project is to train pre- and post-doctoral fellows in cancer research. Role: PI

Foundation grant Cigarroa (PI) 05/01/2015 – 12/31/2017

Clayton Foundation for Research

The major goals are to establish hepatocellular carcinoma (HCC) cell lines and patient-derived xenografts from Hispanic patients and to investigate genetic mutations and gene expression profiles of HCC from Hispanic patients. Role: co-PI

RP170345 Oyajobi (PI) 12/01/2016 – 11/30/2021

Cancer Prevention and Research Institute of Texas (CPRIT)

UTHSCSA Cancer Research Training Program

The major goal of the project is to train undergraduate, pre- and post-doctoral fellows, and post-residency oncology fellows in cancer research. Role: Mentor for Trainee: Xiang Gu

Introduction of research projects in the laboratory of Dr. LuZhe Sun

I. Liver Cancer Research with Genomic Approaches

Hepatocellular carcinoma (HCC) is the major type of malignancy of the liver. It is the third leading cause of cancer death worldwide with over 500,000 people diagnosed each year. In the US, over 28,000 new cases of liver cancer are diagnosed and over 20,000 people die from liver cancer each year. Sadly, there are limited treatment options for HCC and its prognosis is often dismal unless patients are candidates for liver transplantation. According to published research, the incidence and mortality rates in the US are about three times as high in Hispanics as in nonHispanic whites in both genders. Although the genomic and epigenomic alterations in HCC have been reported for Asian and Caucasian patient cohorts, there has been no report for Hispanic patients. Our lab is collaborating with surgeons, radiologists, medical oncologists, and pathologies to collect HCC tumors, tumor-adjacent normal liver tissues, and blood cells from Hispanic patients in South Texas. The tumor tissues have been used to develop novel HCC cell lines and tumor xenografts in mice. We have also identified novel mutated genes, altered gene transcripts, and signaling pathways by performing deep sequencing of DNA and RNA samples and comparisons between tumor and normal samples. We are currently using molecular and cell biology techniques, mouse models of HCC, and bioinformatics approaches to investigate the functions of these genes and pathways in association with obesity in driving HCC development and progression. This project is supported by a grant from Clayton Foundation for Research.

II. Role of Mammary Stem and Progenitor Cells in Early Breast Tumorigenesis

Cancer incidence rises exponentially during mid to late life in humans and in mice. However, the knowledge regarding the cellular and molecular basis that links age with clinical manifestation of breast cancer is scanty. Yet, aging population is steadily expanding in many countries including the US. We recently published that the percentage of mammary stem cells (MaSCs), which are defined to have ability to form basal-like mammospheres in vitro and to regenerate mammary ducts in vivo, increased steadily with age in mouse mammary gland. This was apparently due to increased mammary ducts with hyperplasia and dysplasia and the formation of abnormal MaSCs in the luminal layer of the old mouse mammary gland ducts with early neoplastic lesions. Similar observations were made in old (>60 years) normal human breast tissues in comparison to young (<40 years) ones. Deep sequencing of RNA samples from basal and luminal cells of young and old mouse mammary glands revealed increased inflammation and immune response functions in the old MaSCs suggesting that the aging-associated inflammation and immune reactions may induce the formation of the abnormal MaSCs, which can form early tumorigenic lesions. We are currently testing this hypothesis and investigating the molecular mechanisms that cause the formation of the abnormal MaSCs and potential drugs that can prevent the formation of the abnormal MaSCs. Our studies will establish a foundation for future clinical studies for the prevention of age-related breast cancer, which should particularly benefit the population at high risk for invasive breast cancer. This project is supported by a five-year grant from National Cancer Institute of National Institutes of Health.

Two Xiangya Medical students have successfully completed their two-year research program in my lab. One Xiangya Medical student is currently conducting his research in my lab.